Notice of Allowability	Application No.	Applicant(s)	
	09/508,516	BEBBINGTON ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *12-11-03 and 1-6-04*.

2. ☒ The allowed claim(s) is/are *1,5,6,9-11,14-17,21,22,47,49-51,53-55,57 and 59-79*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☒ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date 3-12-04.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Anne-Marie Yvon on 3-12-04.

The application has been amended as follows:

Claims 80-83 have been canceled.

In claim 1, the phrase "...whereby the first NOI is spliced out of RNA transcribed from the retroviral vector" been change to -- ...whereby the first NOI is capable of being spliced out of RNA when transcribed from the retroviral vector—

In claim 57, the phrase "...whereby the first NOI is spliced out of RNA transcribed from the retroviral vector" been change to -- ...whereby the first NOI is capable of being spliced out of RNA when transcribed from the retroviral vector—

A brief summary of the invention:

The invention involves a retroviral vector having splice donors and acceptors and coding regions capable of being spliced out. The retroviral pro-

vector has a 5' and 3' LTR, a splice donor in the 3' LTR but not in the 5' LTR, a splice acceptor, a packaging signal, and at least one nucleic acid of interest (NOI) (Fig. 27c, 1st of 4 vectors) and is used to transfect packaging cells. A selectable marker may be used as an NOI to select packaging cells that have been successfully transfected. The packaging signal signals the production of viral particles in the packaging cells; the viral particles comprise the pro-viral RNA (the 2nd of 4 vectors in Fig. 27c). The retroviral particles are used to infect target cells. The retroviral vector integrates into the target cell DNA (Fig. 27c, 3rd of 4 vectors). The viral DNA integrated into the genome of the target cell now has a splice donor in both the 5' and 3' LTR. During transcription of the integrated viral DNA in the target cell the first NOI, flanked by the 5' LTR (now having a splice donor) and the splice acceptor, is spliced out (4th of 4 vectors in Fig. 27c).

A summary of the claims:

Claim 1 requires a 5' and 3' LTR, wherein the 5' LTR has a splice donor, a first and second NOI, wherein the first NOI is flanked upstream by the splice donor and flanked downstream by a splice acceptor and a second NOI downstream of the splice acceptor and upstream of the 3' LTR. The first NOI would be the sequence spliced upon transcription of viral DNA integrated into the target cell genome. Claim 1 is limited to the vector once it has been integrated into the host cell but before it has been transcribed into RNA and spliced (3rd

vector of Fig. 27c) because it has a 5' LTR with a splice donor and still has the first NOI.

Claim 47 is directed toward methods of making a retroviral vector having a functional splice donor site in the 5' LTR. The method requires transfecting a packaging cell with a retroviral vector, producing retroviral particles, infecting target cells with the viral particles and obtaining a retroviral vector with a functional splice donor in its 5' LTR.

Claim 57 requires a 5' and 3' LTR, wherein the 5' LTR has a splice donor, a splice acceptor downstream of the splice donor, an NOI downstream of the splice acceptor and upstream of the 3' LTR, and an "intervening sequence" between the splice donor and splice acceptor. The "intervening sequence" would be the sequence spliced upon transcription of viral DNA integrated into the target cell genome. Claim 57 is limited to the vector once it has been integrated into the host cell but before it has been transcribed into RNA and spliced (3rd vector of Fig. 27c) because it has a 5' LTR with a splice donor and still has the "intervening sequence."

Claims 47 and 74 are directed toward methods of making a retroviral vector having a functional splice donor site in the 5' LTR. The methods requires transfecting a packaging cell with a retroviral vector, producing retroviral particles, infecting target cells with the viral particles and obtaining a retroviral vector with a functional splice donor in its 5' LTR. The methods differ in the language used to describe the vector introduced into the packaging cells.

The following is an examiner's statement of reasons for allowance:

The rejection regarding cryptic splice sites in the office action of 2-19-03 was overcome by applicants' arguments provided 7-14-03.

The rejection regarding a first NOI that is a selectable marker has been withdrawn in view of applicants' arguments filed 12-11-03. Packaging cells successfully transfected with the pro-viral vector could be screened be using other methods known in the art, e.g. single cell cloning, and "RNA dot blot."

The rejection regarding the packaging signal as being an essential element of the invention has been withdrawn as it relates to claims 47 and 74 in view of the addition of the packaging signal limitation.

The rejection regarding the packaging signal as being an essential element of the invention is maintained as it relates to claims 1, 57, 80 and 82 has been withdrawn because the specification states non-viral vector systems may be used to deliver the vector to target cells (pg 36, lines 1-11).

Drawings

In Fig. 27c, the non-functional and functional splice donors are mislabeled. A corrected drawing should be provided.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at 571-272-0738.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on 571-272-0804.

The official fax number for this Group is (703) 872-9306.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER